At page 39:

line 22, delete "speciment" and insert -- specimen -- in place thereof.

**In The Claims:**

Sub C'

1. (Amended) A method of modifying a selected gene in cells of a human ~~skin [at~~ one or more locations] in vivo which comprises delivering to said cells ~~at one or more locations~~ of the human skin an effective amount of a composition ~~[comprising]~~ sufficient to bring about stable genetic modifications in the selected gene wherein the composition comprises a chimeric RNA-DNA oligonucleotide and a pharmaceutically acceptable carrier such that [the stable] said genetic modifications are made to the selected gene which result in phenotypic changes at said locations of the human skin wherein the [selected gene is naturally expressed in cells of the human skin] chimeric RNA-DNA oligonucleotide has a double hairpin structure with pyrimidine loops.

B'

C'

4. (Amended) The method of claim 1, wherein the selected gene is ~~tyrosinase~~, COL7A1, LAMA3, LAMB3, LAMC2, COL17A1, ITGA6, ~~ITGB4~~, PLEC1, KRT5, KRT14, PKP1, KRT1, KRT10, KRT9, KRT16, ~~LOR~~, KRT2e, KRT6a, KRT 16, KRT 17, STS, TGM1, GJB2, GJB3, ATP2A2, ~~DSP~~, DSG1, HR, hHB1, hHB6, PAX3, TYR, TYRP-1, OCA2, OA1, MITF, ~~HPS~~, FECH, UROS, URO-D, XPA, XPB, XPC, XPD, XPG, CSB, PTC, STK11/LKB1, PTEN, PTEN, XPB, XPD, WHN, GLA, ATM, ENG, ALK-1, [or] PPO, BPAG2, or DSG3 gene.

B2

Sub C2

8. (Amended) The method of claim 1, wherein the chimeric RNA-DNA oligonucleotide comprises:

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(a) a first string of nucleotides wherein the first string is ~~made~~ of at least four contiguous deoxyribonucleotides flanked on each side ~~by~~ at least nine ribonucleotides; and

(b) a second string of [nucleotides] deoxyribonucleotides that is fully complementary to the first string of nucleotides [~~or~~ is fully complementary to the first string of nucleotides except that the first and second strings have one mismatched base pair in the region corresponding to the said contiguous deoxyribonucleotides of the first string, wherein the second string has the same number of deoxyribonucleotides as in the first string of nucleotides], and

wherein [one or more nucleotides of] the chimeric RNA-DNA oligonucleotide [are] is, nuclease protected, and wherein the chimeric RNA-DNA oligonucleotide has contiguous nucleotides in each of the first and second strings that are fully complementary to a segment of DNA of the selected gene except that the first string has one mismatching deoxyribonucleotide in said contiguous deoxyribonucleotides that defines [the] a site of modification in the selected gene.

9. (Amended) The method of claim 1, wherein the chimeric RNA-DNA oligonucleotide comprises:

(a) a first string of nucleotides wherein the first string is made of at least 20 ribonucleotides; and

(b) a second string of deoxyribonucleotides having the same number of deoxyribonucleotides as in the first string of nucleotides, wherein the second string is fully complementary to the first string of nucleotides except that the second string has a deoxyribonucleotide that forms a mismatched base pair with the corresponding nucleotide in the first string, and

B3

wherein [one or more nucleotides of] the chimeric RNA-DNA oligonucleotide [are] is nuclease protected, and wherein the chimeric RNA-DNA oligonucleotide has contiguous nucleotides in each of the first and second strings that are fully complementary to a segment of [the two strands of] DNA of the selected gene except that the deoxyribonucleotide in the second string also forms a mismatched base pair with the corresponding deoxyribonucleotide in the DNA strand of the selected gene which mismatched base pair defines [the] a site of modification in the selected gene.

10. (Amended) The method of claim 1, wherein the chimeric RNA-DNA oligonucleotide comprises:

(a) a first string of nucleotides wherein the first string is made of at least four contiguous deoxyribonucleotides flanked on each side by at least nine ribonucleotides; and

(b) a second string of [nucleotides] deoxyribonucleotides that is fully complementary to the first string of nucleotides [or is fully complementary to the first string of nucleotides

except that the first and second strings have one mismatched base pair in the region corresponding to the deoxyribonucleotides of the first string, wherein the ~~second~~ string has the same number of deoxyribonucleotides as in the first string ~~of nucleotides~~], and

B3 wherein [one or more nucleotides of] the chimeric RNA-DNA oligonucleotide [are] is nuclease protected, and wherein the chimeric RNA-DNA oligonucleotide has contiguous nucleotides in each ~~of the~~ first and second strings that are fully complementary to a segment of DNA of the selected gene except that the first and second strings have one, two or four pairs of nucleotide insertions or deletions that defines [the] a site of modification in the selected gene.

Sub C2 18. (Amended) A method of modifying a selected gene in cells of an animal skin in vivo [at one or more locations] which comprises delivering to said cells at one or more locations of the animal skin an effective amount of a composition comprising a chimeric RNA-DNA oligonucleotide having a double hairpin structure with pyrimidine loops and a pharmaceutically acceptable carrier such that the stable genetic modifications are made to the selected gene which result in phenotypic changes at said locations of the animal skin, wherein the animal is [selected from the group consisting of] a mouse[, a rabbit, a goat, a monkey, a pig and a cow].

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Sub C3 19. (Amended) The method of claim [17] 18, wherein the selected gene is tyrosinase, COL7A1, LAMA3, LAMB3, LAMC2, COL17A1, ITGA6, ITGB4, PLEC1, ~~KRT5~~, KRT14, PKP1, KRT1, KRT10, KRT9, KRT16, LOR, KRT2, ~~KRT6, KRT~~ 16, KRT 17, STS, TGM1, GJB2, GJB3, ATP2A2, DSP, DSG1, HR, ~~hHB1~~, hHB6, PAX3, TYR, TYRP-1, OCA2, OA1, MITF, HPS, FECH, UROS, ~~URO-D~~, PPO, XPA, XPB, XPC, XPD, XPG, CSB, PTC, STK11/LKB1, ~~PTEN~~, PTEN, XPB, XPD, WHN, GLA, ATM, ENG, ALK-1, [or] a cytokine BPAG2 or DSG3 gene.

Sub C4 23. (Amended) The method of claim 18, wherein the chimeric RNA-DNA oligonucleotide comprises:

B5 (a) a first string ~~of nucleotides~~ wherein the first string is made of at least four contiguous deoxyribonucleotides flanked on each side by at least nine ribonucleotides; and

(b) a second string of [nucleotides] deoxyribonucleotides that is fully complementary to the first string of nucleotides [or is fully complementary to the first string of nucleotides except that the first and second strings have one mismatched base pair in the region corresponding to the deoxyribonucleotides of the first string, wherein the second string has the same number of deoxyribonucleotides as in the first string of nucleotides], and

wherein [one or more nucleotides of] the chimeric RNA-DNA oligonucleotide [are] is nuclease protected, and wherein the chimeric RNA-DNA oligonucleotide has contiguous nucleotides in each of the first and second strings that are fully complementary to a segment of DNA of the selected gene except that the first string has one mismatching deoxyribonucleotide in said contiguous deoxyribonucleotides that defines [the] a site of modification in the selected gene.

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24. (Amended) The method of claim 18, wherein the chimeric RNA-DNA oligonucleotide comprises:

(a) a first string of nucleotides wherein the first string is made of at least 20 ribonucleotides; and

(b) a second string of deoxyribonucleotides having the same number of deoxyribonucleotides as in the first string of nucleotides, wherein the second string is fully complementary to the first string of nucleotides except that the second string has a deoxyribonucleotide that forms a mismatched base pair with the corresponding nucleotide in the first string to make the genetic modifications in the selected gene, and

wherein [one or more nucleotides of] the chimeric RNA-DNA oligonucleotide [are] is nuclease protected, and wherein the chimeric RNA-DNA oligonucleotide has contiguous nucleotides in each of the first and second strings that are fully complementary to a segment of [the two strands of] DNA of the selected gene except that the deoxyribonucleotide in the second string also forms a mismatched base pair with the corresponding deoxyribonucleotide in the DNA strand of the selected gene which mismatched base pair defines [the] a site of modification in the selected gene.

25. (Amended) The method of claim 18, wherein the chimeric RNA-DNA oligonucleotide comprises:

(a) a first string of nucleotides wherein the first string is made of at least four contiguous deoxyribonucleotides flanked on each side by at least nine ribonucleotides; and

(b) a second string of [nucleotides] deoxynribonucleotides that is fully complementary to the first string of nucleotides [or is fully complementary to the first string of nucleotides except that the first and second strings have one mismatched base pair in the region corresponding to the deoxyribonucleotides of the first string, wherein the second string has the same number of deoxyribonucleotides as in the first string of nucleotides], and

wherein [one or more nucleotides of] the chimeric RNA-DNA oligonucleotide [are] is nuclease protected, and wherein the chimeric RNA-DNA oligonucleotide has nucleotides in each of the first and second strings that are fully complementary to a segment of DNA of the selected gene except that the first and second strings have one, two or four pairs of nucleotide insertions or deletions that defines [the] a site of modification in the selected gene.

32. (Amended) An animal model having a skin disorder at one or more locations of its skin wherein the skin disorder is a result of a treatment at said locations with a composition comprising a chimeric RNA-DNA oligonucleotide having a double hairpin structure with pyrimidine loops targeted to a selected skin gene, said oligonucleotide thereby causing a mutation in the selected skin gene which mutation leads to the skin disorder, wherein the skin disorder is an epidermal fragility disorder, a keratinization disorder or albinism disorder.

33. (Amended) The animal model of claim 32, wherein the selected skin gene is Tyr, COL7A1, LAMA3, LAMB3, LAMC2, COL17A1, ITGA6, ITGB4, PLEC1, KRT5, KRT14, PKP1, KRT1, KRT10, KRT9, KRT16, LOR, 1998, KRT2e, KRT6a, KRT 16, KRT 17, STS, TGM1, GJB2, GJB3, ATP2A2, DSP, DSG1, HR, hHB1, hHB6, PAX3, TYR, TYRP-1, OCA2, OA1, MITF, HPS, FECH, UROS, URO-D, PPO, XPA, XPB, XPC, XPD, XPG, CSB, PTC, STK11/LKB1, PTEN, PTEN, XPB, XPD, WHN, GLA, ATM, ENG, ALK-1, [or] a cytokine BPAG2 or DSG3 gene.

34. (Amended) The [method] animal model of claim 33, wherein the selected gene is Tyr gene.

35. (Amended) The [method] animal model of claim 33, wherein the selected gene is COL7A1 gene.

36. (Amended) The [method] animal model of claim 33, wherein the selected gene is KRT17 gene.

37. (Amended) The [method] animal model of claim 32, wherein the skin disorder is due to generation of a mutation in the selected skin gene.

38. (Amended) The [method] animal model of claim 37, wherein the mutation is a point mutation or a frame shift mutation.

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39. (Amended) The [method] animal model of claim 37, wherein the mutation is a dominant mutation.

Subject

40. (Amended) A method of correcting a mutation in a tyrosinase gene in cells of a mammalian skin in vivo [at one or more locations] which comprises delivering to said cells at one or more locations of the mammalian skin an effective amount of a composition comprising a Tyr-A RNA-DNA oligonucleotide for causing stable genetic correction in the tyrosinase gene and a pharmaceutically acceptable carrier such that the correction results in restoration of tyrosinase enzyme activity at said locations of the mammalian skin, wherein the mammalian skin is selected from the group consisting of a [human, a mouse, a rabbit, a goat, a monkey, a pig and a cow] human and a mouse.